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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,356	02/05/2004	Leslie P. Weiner	23714-07992	6800

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,356	WEINER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,11-19,23,26,28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,11-19,23,26,28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 6/15/06 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment remarks filed 6/15/06 have been entered.

2. Claims 8, 9, 11-19, 23, 26, 28, and 30 are pending and under examination.

3. In view of Applicant's amendment, the previous objections to the specification have been withdrawn. Additionally, the previous rejections of Claims 24 and 25 under the first paragraph of 35 U.S.C. 112 (for inadequate written description, new matter), have also been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24, 25, and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) The method comprising the specific steps set forth in Claim 30.

Applicant's arguments, filed 6/15/06 have been fully considered but they are not persuasive. Applicant argues that Example 1 supports the method of the claim.

Applicant is advised that, in general, a specific example cannot likely support a claim comprising a generic method. In this instance, the claim begins by "obtaining a polyclonal mixture of T cells". For support Applicant cites the example wherein PBMCs from four SPMS patients are obtained by leukophoresis. Clearly the specific example cannot support the broader scope of the claim. Likewise, the establishing of autoreactive T cell lines by culture in serum-free media supplemented with gentamicin cannot support the "culturing polyclonal mixture of T cells" recited in the claim.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 8, 9, 11, 12, 14 and 15 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Stinissen et al. (1996).

As set forth previously, Stinissen et al. teaches a method of mediating an immune response comprising administering subcutaneously irradiation-attenuated T-cells derived from autologous peripheral mononuclear cells (comprising T cells) cultured in the presence of natural or synthetic myelin proteins (see particularly page 503, T CELL VACCINATION IN MS).

Applicant's arguments, filed 6/15/06 have been fully considered but they are not persuasive. Applicant argues that the amended claims recite a method not taught by the reference, in particular the reference does not employ the whole bovine myelin proteins or synthetic human myelin proteins of the claims.

The instant claims recite a method of treating a human employing a product by process. In such instances, the process by which the product is made is not considered to add patentability to the method of treating. Accordingly, as the reference teaches a method of mediating an immune response comprising administering T cells, in this case cultured in the presence of human myelin proteins, the method of the reference is the method of the instant claims.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 16-19 stand rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996).

As set forth previously, Stinissen et al has been discussed above. The reference differs from the claimed invention only in that it does not teach the optimization of the claimed method as set forth in dependent Claims 16-19. For example, the choice of dosage (Claim 17), and timing (Claim 16), would have fallen well within the purview of the skilled artisan at the time of the invention. Regarding the increasing of the dosages as set forth in Claims 18 and 19, one of ordinary skill in the art at the time the invention was made would have been well aware of the concept of increasing dosage if no response is obtained up to the point of efficacy or adverse reaction. These limitations do not render the claimed method patentably distinct.

Applicant's arguments, filed 6/15/06 have been fully considered but they are not persuasive. Applicant argues that as Stinissen et al. is deficient the rejection should be withdrawn.

See the Examiner's response in Section 7 above.

10. Claim 13 stands rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996) in view of Correale et al (1995).

As set forth previously, Stinissen et al. has been discussed above. The reference further teaches that MBP is not the only autoantigen candidate in MS. The reference teaches that additional antigens, including PLP, MAG, and MOG might also be the targets of autoreactive T cells (see particularly page 501, column 1, second full paragraph).

The reference differs from the claimed invention only in that it does not teach the use of attenuated T cells that target more than one myelin protein.

Correale et al. extends the teachings of Stinissen et al. regarding additional MS autoantigens. The reference teaches that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus, broadening the autoimmune response (see particularly page 1375, last paragraph - page 1376, first paragraph.

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform the method of administering attenuated T cells, as taught by Stinissen et al., employing attenuated T cells autoreactive to multiple myelin antigens. One of ordinary skill in the art at the time the invention was made would have been motivated to employ attenuated T cells autoreactive to multiple myelin antigens given the teachings of Stinissen et al. that MBP is not the only autoantigen candidate in MS and extended by Correale et al. that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus broadening the autoimmune response.

Applicant's arguments, filed 6/15/06 have been fully considered but they are not persuasive. Applicant argues that Correale et al. does not remedy the defects of Stinissen et al. and that the combination does not include all of the elements of the claims.

It is unclear precisely which elements of the claims are missing from the combined references. Accordingly the rejection has been maintained.

11. The following are new grounds for rejection.

12. Claims 8, 9, 11-19, 23, 26, 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) … T cells are cultured in the presence of whole bovine myelin proteins or synthetic human proteins … (Claims 8 and 30).

B) … T cells that respond to a plurality of different myelin proteins (Claim 11).

C) … T cells are reactive to a plurality of different myelin proteins (Claim 23).

Regarding A), Applicant cites page 8 of the specification for support.

At page 8 the specification discloses PBMCs are cultured in the presence of cow myelin proteins or synthetic complete human

proteins.

Regarding B) and C), Applicant cites pages 8 and 11 of the specification for support.

At page 8 the specification discloses PBMCs are cultured in the presence specific myelin antigens. Page 11 discloses a specific example in which PBMCs and myelin antigens are employed.

12. Claims 8, 9, 11-19, 23, 26, 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding *in vivo* methods which rely on previously undescribed and generally unpredictable mechanisms, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)." The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an

enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims encompass the use of attenuated T cells for mediating an immune response in an MS patient. Presumably, an immune response is mounted against attenuated T cells specific for MS-associated antigens, after which the newly generated response reduces the number of aberrant autoimmune T cells in the MS patient.

A review of the claims reveals that, except for Claim 11, the claimed method need not employ T cells specific for, or that even respond to, any MS-associated antigens. Indeed, the method need not even limited to the use of human T cells. It is also noted that the method also does not require the reduction of the aberrant autoimmune response. As it is unlikely that *any* T cell "mediating" *any* sort of immune response would provide an effective treatment for MS, it is clear that practicing the breadth of the claimed invention would require undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, the lack of sufficient working examples, the unpredictability of the art, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

8/1/06

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